REMARKS

Status of the Claims

Claims 1, 14-17, 19, 21-23, 38 and 54-76 are pending in the application.

Claims 1, 14-17, 19, 21-23, 38 and 54-76 were rejected.

Claims 1, 21, 61-63, 73, 74 have been amended. Claim 77 has been added.

Upon entry of this amendment, claims 1, 14-17, 19, 21-23, 38 and 54-77 will be pending.

Summary of the Amendment

Claims 1, 21-23, 55, 61-63, 73, and 74 have been amended to correct obvious typographical errors per the Office request. The claims as amended are more grammatically correct.

Claim 1 has been amended to add types of immunomodulating proteins disclosed in the application. Support for the amendment appear throughout the specification and claims as originally filed, but particularly on pages 13, 14, 56-62, and 67-80 of the specification.

New claim 77 has been added to recite a subgenus of the claimed invention. Support for the amendment appear throughout the specification and claims as originally filed, but particularly on pages 13 and 14 of the specification.

No new matter has been added.

Claim Objections

Claims 1, 21, 22, 23, 55, 61-63, 73, and 74 have been objected to for reciting obvious typographical errors. Per the Office request, Applicants have amended claims 1, 21, 22, 23, 55, 61-63, 73, and 74 to correct the obvious typographical errors. Applicants respectfully request that the objection to the claims be withdrawn.

Claim Rejection Under 35 U.S.C. § 112, first paragraph

Claims 21-23, 54, 61-63, 65, 72-74, and 76 stand rejected under 35 U.S.C. §112, first paragraph, for allegedly failing the enablement requirement. The Office asserts that:

> while [the specification] is enabling for a composition comprising an isolated nucleic acid molecule, wherein the isolated nucleic acid molecule comprises a nucleic acid sequence consisting of a nucleic acid sequence that encodes a fusion protein that consists of either a non-IgE protein or an immuno-modulating protein sequence linked to an IgE signal peptide, [the specification] does not reasonably provide enablement for (1) any pharmaceutical composition or (2) any DNA vaccine for generation of a protective immunity against the infection of a pathogen or against the development of a disease.

(Office Action, page 4). More specifically, the Office asserts that the specification does not enable an ordinary person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with the claims. Applicants traverse the rejection and respectfully request the rejection be withdrawn.

As a preliminary matter, Applicants direct the Office to ongoing clinical trials in which the constructs of the present invention are being tested for efficiency in human beings. On October 18, 2008, the Applicants, in collaboration with others, initiated a study registered with the Food and Drug Administration using nucleic acid constructs that encode a fusion protein IgE-leader sequence and a non-IgE protein sequences. Applicants note that information related to the clinical trial may be furnished to the Office upon request. Applicants respectfully note that the threshold for patentability of an invention is lower than the threshold for FDA approval.

The specification discloses immunization protocols that include the administration of nucleic acid sequences that encode a fusion protein consisting of an IgE-leader sequence and a non-IgE protein sequence. The data illustrate that T cells from HIV-1 infected patients can be expanded by administration of the nucleic acid constructs (Specification, page 47). The data illustrate that the expansion is antigen-specific (Specification, page 46-50). The data illustrate that IL-15 expression enhances antigen-specific immune responses by imparting memory of CD8+ T cells (Specification, page 55). Increasing the expression of immunomodulating proteins likely enhances the effects of cytokine on demonstrate that the nucleic acid constructs of the present invention express either immunogen or immunomodulating proteins at levels dramatically higher than nucleic acid constructs that encode protein without the IgE leader sequence. The higher expression was shown to increase antigen expression or

immunomodulating protein expression in cells originating from different species (see Figure 12 and page 42). The same DNA constructs also enhance the immune response of mice when administered as compared to negative controls (Examples Section and Figures 15-16 with accompanying text).

Belakova, *et. al.*, specifically states that:

> the two most critical factors for current DNA vaccines are (1) the efficiency with which the DNA vector reaches the target cell nuclei (transfection efficacy) and (2) the amount of actual protein synthesized in DNA vaccine-transfected cells.

The claimed invention addresses the concerns related to increased expression of antigen and immunomodulating protein by the use of the encoded IgE leader sequence. Nowhere in Belakova, Hu, Mittendorf, or Ulmer do authors question the efficacy of vaccines that utilize DNA constructs that express the fusion proteins of the claimed invention. Nowhere in Belakova, Hu, Mittendorf, or Ulmer do authors question the efficacy of DNA constructs with Ig leader sequences that increase the expression of immunomodulating proteins to the degree necessary to enhance the immune response. Therefore, the cited references are largely irrelevant to casting any doubt on whether the claimed invention is enabled. In fact, the references suggest the contrary position. Ulmer, for example, specifically discloses that due to the recent commercialization of two different DNA vaccines, "DNA vaccines are a viable technology, and their diversity of applications attests the versatility of this technology." (Ulmer, page 221, concluding paragraph).

Applicants submit that the initiation of a clinical trial in connection with the *in vitro* and *in vivo* data submitted with the application provide one of ordinary skill in the art with sufficient guidance to make and use the claimed invention commensurate in scope with the claims as amended. Furthermore, the evidence cited by the Office which allegedly cast doubt on the enablement of the invention fails to establish a *prima facie* case for lack of enablement of the claimed invention. Applicants respectfully request withdrawal of the rejection of claims 21-23, 54, 61-63, 65, 72-74, and 76 under 35 U.S.C. §112, first paragraph, be withdrawn.

Claim Rejection Under 35 U.S.C. § 102

Claims 1, 14-17, 19, 21-23, 38, and 54-76 stand rejected under 35 U.S.C. 102(a) and 102(e) as allegedly being anticipated by Weiner, *et. al.*, US 2002/0123099 A1 (hereinafter "Weiner"). Applicants traverse the rejection and respectfully request that the rejection be withdrawn.

In order to anticipate the claims, the cited reference must disclose each an every limitation of the claims. As amended, claim 1 recites:

> An isolated nucleic acid molecule comprising a nucleic acid sequence selected from the group consisting of:
>
> a nucleic acid sequence that encodes a fusion protein that consists of a non-IgE protein sequences linked to a IgE signal peptide that is from the same species as the non-IgE protein; and
>
> a nucleic acid sequence that encodes a fusion protein that consists of a non-IgE protein sequences linked to a IgE signal peptide ***wherein the non-IgE protein is an immunomodulating protein selected from the group consisting of cytokines, chemokines, cellular death receptors, cellular adhesion molecules, cellular growth factors, cellular growth factor receptors, protein kinases and enzymes or functional fragment thereof.***

(emphasis added). The amendment obviates the basis of rejection. Applicants respectfully request that the rejection of claims 1, 14-17, 19, 21-23, 38, and 54-76 based upon 35 U.S.C. § 102(a) and 102(e) be withdrawn.

Claims 1, 14, 16, 17, 19, 21, 22, 38, 54-56, 58-62, 64-67, 69-73, 74, and 76 stand rejected under 35 U.S.C. 102(b) as allegedly being anticipated by Yang, *et. al.*, *Journal of Infectious Disease*; 184(7): 809-16, 2001 (hereinafter "Yang 1"). Claims 1, 14, 16, 17, 19, 21, 22, 38, 54-56, 58-62, 64-67, 69-73, 74, and 76 stand rejected under 35 U.S.C. 102(b) as allegedly being anticipated by Yang, *et. al.*, *Journal of Infectious Disease*; 184(7): 809-16, 2001 (hereinafter

"Yang 2"). Applicants traverse the rejections and respectfully request that the rejections be withdrawn.

The amendment to claim 1 obviates the basis of rejection. Neither Yang 1 nor Yang 2 disclose every limitation of the claims. Therefore, the references do not anticipate the claims. Applicants respectfully request that the rejection of claims 1, 14, 16, 17, 19, 21, 22, 38, 54-56, 58-62, 64-67, 69-73, 74, and 76 based upon 35 U.S.C. § 102(b) be withdrawn.

Conclusion

Claims 1, 14-17, 19, 21-23, 38 and 54-77 are in condition for allowance. A notice of allowance is earnestly solicited. Applicants invite the Examiner to contact the undersigned at 610.640.7852 to clarify any unresolved issues raised by this response.

The Commissioner is hereby authorized to charge any deficiencies of fees and credit of any overpayments to Deposit Account No. 50-0436.

Respectfully Submitted,

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